General

Guideline Title

Prostate cancer: diagnosis and treatment.

Bibliographic Source(s)

National Collaborating Centre for Cancer. Prostate cancer: diagnosis and treatment. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Jan. 46 p. (Clinical guideline; no. 175).

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Collaborating Centre for Cancer. Prostate cancer: diagnosis and treatment. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Feb. 146 p. (NICE clinical guideline; no. 58).

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Recommendations are marked as [new 2014], [2014], [2008] or [2008, amended 2014]:

- [new 2014] indicates that the evidence has been reviewed and the recommendation has been added or updated
- [2014] indicates that the evidence has been reviewed but no change has been made to the recommended action
- [2008] indicates that the evidence has not been reviewed since 2008
- [2008, amended 2014] indicates that the evidence has not been reviewed since 2008, but changes have been made to the recommendation wording that change the meaning

Information and Decision Support for Men with Prostate Cancer, Their Partners and Carers

Information

Follow the recommendations on communication and patient-centred care in the NICE cancer service guidance Improving outcomes in urological cancers and Improving supportive and palliative care for adults with cancer throughout the patient journey. [2008]

Offer men with prostate cancer individualised information tailored to their own needs. This information should be given by a healthcare professional (for example, a consultant or specialist nurse) and may be supported by written and visual media (for example, slide sets or DVDs). [2008]

Offer men with prostate cancer advice on how to access information and support from websites, local and national cancer information services, and from cancer support groups. [2008]

Before choosing or recommending information resources for men with prostate cancer, check that their content is clear, reliable and up to date. Seek feedback from men with prostate cancer and their carers to identify the highest quality information resources. [2008]

Decision Support

Ascertain the extent to which the man wishes to be involved in decision-making and ensure that he has sufficient information to do so. [2008]

Use a validated, up-to-date decision aid[1] in all urological cancer multidisciplinary teams (MDTs). Healthcare professionals trained in its use should offer it to men with localised prostate cancer when making treatment decisions. [2008]

Nomograms may be used by healthcare professionals in partnership with men with prostate cancer to:

- Aid decision-making
- Help predict biopsy results
- Help predict pathological stage
- Help predict risk of treatment failure [2008]

When nomograms are used, clearly explain the reliability, validity and limitations of the prediction. [2008]

Discuss all relevant management options recommended in this guideline with men with prostate cancer and their partners or carers, irrespective of whether they are available through local services. [2008]

Tell men:

- About treatment options and their risks and benefits[1] in an objective, unbiased manner and
- That there is limited evidence for some treatment options [new 2014]

Ensure that mechanisms are in place to allow men with prostate cancer and their primary care providers to gain access to specialist services throughout the course of their disease. [2008]

Adequately inform men with prostate cancer and their partners or carers about the effects of prostate cancer and the treatment options on their sexual function, physical appearance, continence and other aspects of masculinity. Support men and their partners or carers in making treatment decisions, taking into account the effects on quality of life as well as survival. [2008]

Offer men with prostate cancer and their partners or carers the opportunity to talk to a healthcare professional experienced in dealing with psychosexual issues at any stage of the illness and its treatment. [2008]

Assessment

Diagnosis

Biopsy

To help men decide whether to have a prostate biopsy, discuss with them their prostate-specific antigen (PSA) level, digital rectal examination (DRE) findings (including an estimate of prostate size) and comorbidities, together with their risk factors (including increasing age and black African-Caribbean family origin) and any history of a previous negative prostate biopsy. Do not automatically offer a prostate biopsy on the basis of serum PSA level alone. [2008]

Give men and their partners or carers information, support and adequate time to decide whether or not they wish to undergo prostate biopsy. Include an explanation of the risks (including the increased chance of having to live with the diagnosis of clinically insignificant prostate cancer) and benefits of prostate biopsy. [2008]

If the clinical suspicion of prostate cancer is high, because of a high PSA value and evidence of bone metastases (identified by a positive isotope bone scan or sclerotic metastases on plain radiographs), do not offer prostate biopsy for histological confirmation, unless this is required as part of a clinical trial. [2008]

Carry out prostate biopsy following the procedure recommended by the Prostate Cancer Risk Management Programme in Undertaking a transrectal ultrasound guided biopsy of the prostate . [2008]

A core member of the urological cancer MDT should review the risk factors of all men who have had a negative first prostate biopsy, and discuss with the man that:

- There is still a risk that prostate cancer is present and
- The risk is slightly higher if any of the following risk factors are present:
  - The biopsy showed high-grade prostatic intra-epithelial neoplasia (HGPIN)
  - The biopsy showed atypical small acinar proliferation (ASAP)
  - Abnormal digital rectal examination [new 2014]

Magnetic Resonance Imaging (MRI) for Rebiopsy

Consider multiparametric MRI (using T2- and diffusion-weighted imaging) for men with a negative transrectal ultrasound 10–12 core biopsy to determine whether another biopsy is needed. [new 2014]

Do not offer another biopsy if the multiparametric MRI (using T2- and diffusion-weighted imaging) is negative, unless any of the risk factors listed in the recommendation above are present. [new 2014]

Staging

Determine the provisional treatment intent (radical or non-radical) before decisions on imaging are made. [2008]

Do not routinely offer imaging to men who are not candidates for radical treatment. [2008]

Offer isotope bone scans when hormonal therapy is being deferred through watchful waiting to asymptomatic men who are at high risk of developing bone complications. [2008]

Consider multiparametric MRI, or computed tomography (CT) if MRI is contraindicated, for men with histologically proven prostate cancer if knowledge of the T or N stage could affect management. [new 2014]

Urological cancer MDTs should assign a risk category (see Table 1, below) to all newly diagnosed men with localised prostate cancer. [2008]

Table 1. Risk Stratification for Men with Localised Prostate Cancer

Level of Risk	Prostate-specific Antigen (PSA)		Gleason Score		Clinical Stage
Low risk	<10 ng/ml	and	≤6	and	T1–T2a
Intermediate risk	10–20 ng/ml	or	7	or	T2b
High risk*	>20 ng/ml	or	8–10	or	≥T2c

*High-risk localised prostate cancer is also included in the definition of locally advanced prostate cancer.

Do not offer CT of the pelvis to men with low- or intermediate-risk localised prostate cancer (see Table 1, above). [2008]

Do not routinely offer isotope bone scans to men with low-risk localised prostate cancer. [2008]

Do not offer positron emission tomography imaging for prostate cancer in routine clinical practice. [2008]

Localised and Locally Advanced Prostate Cancer

Prior to radical treatment, warn men and, if they wish, their partner, that radical treatment for prostate cancer will result in an alteration of sexual experience, and may result in loss of sexual function. [2008, amended 2014]

Warn men and, if they wish, their partner, about the potential loss of ejaculation and fertility associated with radical treatment for prostate cancer. Offer sperm storage. [2008, amended 2014]

Warn men undergoing radical treatment for prostate cancer of the likely effects of the treatment on their urinary function. [2008, amended 2014]

Offer men experiencing troublesome urinary symptoms before treatment a urological assessment. [2008]

Given the range of treatment modalities and their serious side effects, men with prostate cancer who are candidates for radical treatment should have the opportunity to discuss their treatment options with a specialist surgical oncologist and a specialist clinical oncologist. [2008]

Tell men that there is a small increase in the risk of colorectal cancer after radical external beam radiotherapy for prostate cancer. [new 2014]

Low-risk Localised Prostate Cancer

Active Surveillance

Offer active surveillance (in line with recommendation below) as an option to men with low-risk localised prostate cancer for whom radical prostatectomy or radical radiotherapy is suitable. [new 2014]

Consider using the protocol in Table 2 below, for men who have chosen active surveillance. [new 2014]

Table 2. Protocol for Active Surveillance

Timing	Tests*
At enrolment in active surveillance	Multiparametric magnetic resonance imaging (MRI) if not previously performed
Year 1 of active surveillance	• Every 3–4 months: measure prostate-specific antigen (PSA)† • Throughout active surveillance: monitor PSA kinetics‡ • Every 6–12 months: digital rectal examination (DRE)¶ • At 12 months: prostate rebiopsy
Years 2–4 of active surveillance	• Every 3–6 months: measure PSA† • Throughout active surveillance: monitor PSA kinetics‡ • Every 6–12 months: DRE¶
Year 5 and every year thereafter until active surveillance ends	• Every 6 months: measure PSA† • Throughout active surveillance: monitor PSA kinetics‡ • Every 12 months: DRE¶

*If there is concern about clinical or PSA changes at any time during active surveillance, reassess with multiparametric MRI and/or rebiopsy.

†May be carried out in primary care if there are agreed shared-care protocols and recall systems.

‡May include PSA doubling time and velocity.

¶Should be performed by a healthcare professional with expertise and confidence in performing DRE.

The decision to proceed from an active surveillance regimen to radical treatment should be made in the light of the individual man's personal preferences, comorbidities and life expectancy. [2008]

Radical Treatment

Offer radical treatment to men with localised prostate cancer who have chosen an active surveillance regimen and who have evidence of disease progression. [2008, amended 2014]

Intermediate- and High-risk Localised Prostate Cancer

Active Surveillance

Consider active surveillance for men with intermediate-risk localised prostate cancer who do not wish to have immediate radical prostatectomy or

radical radiotherapy. [new 2014]

Do not offer active surveillance to men with high-risk localised prostate cancer. [2014]

Radical Treatment

Offer radical prostatectomy or radical radiotherapy to men with intermediate-risk localised prostate cancer. [2008]

Offer radical prostatectomy or radical radiotherapy to men with high-risk localised prostate cancer when there is a realistic prospect of long-term disease control. [2008]

Commissioners of urology services should consider providing robotic surgery to treat localised prostate cancer. [new 2014]

Commissioners should ensure that robotic systems for the surgical treatment of localised prostate cancer are cost effective by basing them in centres that are expected to perform at least 150 robot-assisted laparoscopic radical prostatectomies per year. [new 2014]

Offer men undergoing radical external beam radiotherapy for localised prostate cancer a minimum dose of 74 Gy to the prostate at no more than 2 Gy per fraction. [2008]

For men with localised prostate cancer[2] receiving radical external beam radiotherapy with curative intent, offer planned treatment techniques that optimise the dose to the tumour while minimising the risks of normal tissue damage. [2008]

Offer men with intermediate- and high-risk localised prostate cancer a combination of radical radiotherapy and androgen deprivation therapy, rather than radical radiotherapy or androgen deprivation therapy alone. [new 2014]

Offer men with intermediate- and high-risk localised prostate cancer 6 months of androgen deprivation therapy before, during or after radical external beam radiotherapy. [new 2014]

Consider continuing androgen deprivation therapy for up to 3 years for men with high-risk localised prostate cancer and discuss the benefits and risks of this option with them. [new 2014]

Consider high-dose rate brachytherapy in combination with external beam radiotherapy for men with intermediate- and high-risk localised prostate cancer. [new 2014]

Do not offer brachytherapy alone to men with high-risk localised prostate cancer. [2008]

Do not offer high-intensity focused ultrasound and cryotherapy to men with localised prostate cancer other than in the context of controlled clinical trials comparing their use with established interventions.[3] [2008]

Watchful Waiting

A member of the urological cancer MDT should review men with localised prostate cancer who have chosen a watchful waiting regimen and who have evidence of significant disease progression (that is, rapidly rising PSA level or bone pain). [2008]

Locally Advanced Prostate Cancer

Clinical oncologists should consider pelvic radiotherapy in men with locally advanced prostate cancer who have a higher than 15% risk of pelvic lymph node involvement[4] and who are to receive neoadjuvant hormonal therapy and radical radiotherapy. [2008]

Do not offer immediate post-operative radiotherapy after radical prostatectomy, even to men with margin-positive disease, other than in the context of a clinical trial. [2008]

Do not offer adjuvant hormonal therapy in addition to radical prostatectomy, even to men with margin-positive disease, other than in the context of a clinical trial. [2008]

Do not offer high-intensity focused ultrasound and cryotherapy to men with locally advanced prostate cancer other than in the context of controlled clinical trials comparing their use with established interventions.[3] [2008]

Do not offer bisphosphonates for the prevention of bone metastases in men with prostate cancer. [2008]

Managing Adverse Effects of Radical Treatment

Sexual Dysfunction

Ensure that men have early and ongoing access to specialist erectile dysfunction services. [2008, amended 2014]

Offer men with prostate cancer who experience loss of erectile function phosphodiesterase type 5 (PDE5) inhibitors to improve their chance of spontaneous erections. [2008]

If PDE5 inhibitors fail to restore erectile function or are contraindicated, offer men vacuum devices, intraurethral inserts or penile injections, or penile prostheses as an alternative. [2008]

Urinary Incontinence

Ensure that men with troublesome urinary symptoms after treatment have access to specialist continence services for assessment, diagnosis and conservative treatment. This may include coping strategies, along with pelvic floor muscle re-education, bladder retraining and pharmacotherapy. [2008]

Refer men with intractable stress incontinence to a specialist surgeon for consideration of an artificial urinary sphincter. [2008]

Do not offer injection of bulking agents into the distal urinary sphincter to treat stress incontinence. [2008]

Radiation-induced Enteropathy

Ensure that men with signs or symptoms of radiation-induced enteropathy are offered care from a team of professionals with expertise in radiation-induced enteropathy (who may include oncologists, gastroenterologists, bowel surgeons, dietitians and specialist nurses). [new 2014]

The nature and treatment of radiation-induced enteropathy should be included in the training programmes for oncologists and gastroenterologists. [2014]

Carry out full investigations, including flexible sigmoidoscopy, in men who have symptoms of radiation-induced enteropathy to exclude inflammatory bowel disease or malignancy of the large bowel and to ascertain the nature of the radiation injury. Use caution when performing anterior wall rectal biopsy after brachytherapy because of the risk of fistulation. [2014]

Follow-up

Discuss the purpose, duration, frequency and location of follow-up with each man with localised prostate cancer[2], and if he wishes, his partner or carers. [2008]

Clearly advise men with prostate cancer about potential longer-term adverse effects of treatment and when and how to report them. [2008]

Men with prostate cancer who have chosen a watchful waiting regimen with no curative intent should normally be followed up in primary care in accordance with protocols agreed by the local urological cancer MDT and the relevant primary care organisation(s). Their PSA should be measured at least once a year. [2008]

Check PSA levels for all men with prostate cancer who are having radical treatment at the earliest 6 weeks following treatment, at least every 6 months for the first 2 years and then at least once a year thereafter. [2008]

Do not routinely offer DRE to men with localised prostate cancer while the PSA remains at baseline levels. [2008]

After at least 2 years, offer follow-up outside hospital (for example, in primary care) by telephone or secure electronic communications to men with a stable PSA who have had no significant treatment complications, unless they are taking part in a clinical trial that requires formal clinic based follow-up. Direct access to the urological cancer MDT should be offered and explained. [2008]

Managing Relapse After Radical Treatment

Analyse serial PSA levels after radical treatment using the same assay technique. [2008]

Do not offer biopsy of the prostatic bed to men with prostate cancer who have had a radical prostatectomy. [2008]

Offer biopsy of the prostate after radiotherapy only to men with prostate cancer who are being considered for local salvage therapy in the context of a clinical trial. [2008]

For men with evidence of biochemical relapse following radical treatment and who are considering radical salvage therapy:

- Do not offer routine MRI scanning prior to salvage radiotherapy in men with prostate cancer.
- Offer an isotope bone scan if symptoms or PSA trends are suggestive of metastases. [2008]

Biochemical relapse (a rising PSA) alone should not necessarily prompt an immediate change in treatment. [2008]

Biochemical relapse should trigger an estimate of PSA doubling time, based on a minimum of 3 measurements over at least a 6-month period. [2008]

Offer men with biochemical relapse after radical prostatectomy, with no known metastases, radical radiotherapy to the prostatic bed. [2008]

Men with biochemical relapse should be considered for entry to appropriate clinical trials. [2008]

Do not routinely offer hormonal therapy to men with prostate cancer who have a biochemical relapse unless they have:

- Symptomatic local disease progression, or
- Any proven metastases, or
- A PSA doubling time of less than 3 months [2008]

Men Having Hormone Therapy

Consider intermittent therapy for men having long-term androgen deprivation therapy (not in the adjuvant setting), and include discussion with the man, and his partner, family or carers if he wishes, about:

- The rationale for intermittent therapy and
- The limited evidence for reduction in side effects from intermittent therapy and
- The effect of intermittent therapy on progression of prostate cancer. [new 2014]

For men who are having intermittent androgen deprivation therapy:

- Measure PSA every 3 months and
- Restart androgen deprivation therapy if PSA is 10 ng/ml or above, or if there is symptomatic progression. [new 2014]

Managing Adverse Effects of Hormone Therapy

Hot Flushes

Offer medroxyprogesterone[5] (20 mg per day), initially for 10 weeks, to manage troublesome hot flushes caused by long-term androgen suppression and evaluate the effect at the end of the treatment period. [new 2014]

Consider cyproterone acetate or megestrol acetate[6] (20 mg twice a day for 4 weeks) to treat troublesome hot flushes if medroxyprogesterone is not effective or not tolerated. [new 2014]

Tell men that there is no good-quality evidence for the use of complementary therapies to treat troublesome hot flushes. [new 2014]

Sexual Dysfunction

Before starting androgen deprivation therapy, tell men and, if they wish, their partner, that long term androgen deprivation will cause a reduction in libido and possible loss of sexual function. [new 2014]

Advise men and, if they wish, their partner, about the potential loss of ejaculation and fertility associated with long-term androgen deprivation and offer sperm storage. [new 2014]

Ensure that men starting androgen deprivation therapy have access to specialist erectile dysfunction services. [new 2014]

Consider referring men who are having long-term androgen deprivation therapy, and their partners, for psychosexual counselling. [new 2014]

Offer PDE5 inhibitors to men having long-term androgen deprivation therapy who experience loss of erectile function. [new 2014]

If PDE5 inhibitors fail to restore erectile function or are contraindicated, offer a choice of:

- Intraurethral inserts
- Penile injections

- Penile prostheses
- Vacuum devices [new 2014]

Osteoporosis

Do not routinely offer bisphosphonates to prevent osteoporosis in men with prostate cancer having androgen deprivation therapy. [2008]

Consider assessing fracture risk in men with prostate cancer who are having androgen deprivation therapy, in line with the NGC summary of the NICE guideline Osteoporosis: assessing the risk in fragility fracture (NICE clinical guideline 146). [new 2014]

Offer bisphosphonates to men who are having androgen deprivation therapy and have osteoporosis. [new 2014]

Consider denosumab for men who are having androgen deprivation therapy and have osteoporosis if bisphosphonates are contraindicated or not tolerated. [new 2014]

Gynaecomastia

For men starting long-term bicalutamide monotherapy (longer than 6 months), offer prophylactic radiotherapy to both breast buds within the first month of treatment. Choose a single fraction of 8 Gy using orthovoltage or electron beam radiotherapy. [2008]

If radiotherapy is unsuccessful in preventing gynaecomastia, weekly tamoxifen[7] should be considered. [2008]

Fatigue

Tell men who are starting androgen deprivation therapy that fatigue is a recognised side effect of this therapy and not necessarily a result of prostate cancer. [new 2014]

Offer men who are starting or having androgen deprivation therapy supervised resistance and aerobic exercise at least twice a week for 12 weeks to reduce fatigue and improve quality of life. [new 2014]

Metastatic Prostate Cancer

Information and Support

Offer men with metastatic prostate cancer tailored information and access to specialist urology and palliative care teams to address the specific needs of men with metastatic prostate cancer. Offer them the opportunity to discuss any significant changes in their disease status or symptoms as these occur. [2008]

Integrate palliative interventions at any stage into coordinated care, and facilitate any transitions between care settings as smoothly as possible. [2008]

Discuss personal preferences for palliative care as early as possible with men with metastatic prostate cancer, their partners and carers. Tailor treatment/care plans accordingly and identify the preferred place of care. [2008]

Ensure that palliative care is available when needed and is not limited to the end of life. It should not be restricted to being associated with hospice care. [2008]

Offer a regular assessment of needs to men with metastatic prostate cancer. [2008]

Treatment

Offer bilateral orchidectomy to all men with metastatic prostate cancer as an alternative to continuous luteinising hormone-releasing hormone agonist therapy. [2008]

Do not offer combined androgen blockade as a first-line treatment for men with metastatic prostate cancer. [2008]

For men with metastatic prostate cancer who are willing to accept the adverse impact on overall survival and gynaecomastia in the hope of retaining sexual function, offer anti-androgen monotherapy with bicalutamide[8] (150 mg). [2008]

Begin androgen deprivation therapy and stop bicalutamide treatment in men with metastatic prostate cancer who are taking bicalutamide monotherapy and who do not maintain satisfactory sexual function. [2008]

Hormone-relapsed Metastatic Prostate Cancer

Note: Recommendations in this section marked with an asterisk are from Docetaxel for the treatment of hormone-refractory metastatic prostate cancer (NICE technology appraisal guidance 101).

When men with prostate cancer develop biochemical evidence of hormone-relapsed disease, their treatment options should be discussed by the urological cancer MDT with a view to seeking an oncologist and/or specialist palliative care opinion, as appropriate. [2008]

Docetaxel is recommended, within its licensed indications, as a treatment option for men with hormone-refractory prostate cancer only if their Karnofsky performance-status score is 60% or more. [2008]*

It is recommended that treatment with docetaxel should be stopped:

- At the completion of planned treatment of up to 10 cycles, or
- If severe adverse events occur, or
- In the presence of progression of disease as evidenced by clinical or laboratory criteria, or by imaging studies [2008]*

Repeat cycles of treatment with docetaxel are not recommended if the disease recurs after completion of the planned course of chemotherapy. [2008]*

Offer a corticosteroid such as dexamethasone (0.5 mg daily) as third-line hormonal therapy after androgen deprivation therapy and anti-androgen therapy to men with hormone-relapsed prostate cancer. [2008]

Offer spinal MRI to men with hormone-relapsed prostate cancer shown to have extensive metastases in the spine (for example, on a bone scan) if they develop any spinal-related symptoms. [2008]

Do not routinely offer spinal MRI to all men with hormone-relapsed prostate cancer and known bone metastases. [2008]

Bone-targeted Therapies

Do not offer bisphosphonates to prevent or reduce the complications of bone metastases in men with hormone-relapsed prostate cancer. [2008]

Bisphosphonates for pain relief may be considered for men with hormone-relapsed prostate cancer when other treatments (including analgesics and palliative radiotherapy) have failed. Choose the oral or intravenous route of administration according to convenience, tolerability and cost. [2008]

Strontium-89 should be considered for men with hormone-relapsed prostate cancer and painful bone metastases, especially those men who are unlikely to receive myelosuppressive chemotherapy. [2008]

Pelvic-targeted Therapies

Offer decompression of the upper urinary tract by percutaneous nephrostomy or by insertion of a double J stent to men with obstructive uropathy secondary to hormone-relapsed prostate cancer. [2008]

The option of no intervention should also be discussed with men with obstructive uropathy secondary to hormone-relapsed prostate cancer and remains a choice for some. [2008]

Footnotes

[1]A decision aid for men with localised prostate cancer is available from NHS Shared decision making.

[2]This may also apply to some men with locally advanced prostate cancer.

[3]NICE interventional procedure guidance 118, 119 and 145 evaluated the safety and efficacy of cryotherapy and high-intensity focused ultrasound for the treatment of prostate cancer. NICE clinical guidelines provide guidance on the appropriate treatment and care of people with specific diseases and conditions within the NHS. As there was a lack of evidence on quality of life benefits and long-term survival, these interventions are not recommended in this guideline.

[4]Estimated using the Roach formula; %LN risk = 2/3 PSA + (10x [Gleason score – 6]).

[5]At the time of publication (January 2014), medroxyprogesterone did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[6]At the time of publication (January 2014), megestrol acetate did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[7]At the time of publication (January 2014), tamoxifen did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[8]At the time of publication (January 2014), bicalutamide did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

Clinical Algorithm(s)

The following clinical algorithms are provided in the full version of the original guideline document:

- Diagnosis and staging
- Localised prostate cancer
- Treatment for localised prostate cancer
- Biochemical relapse
- Locally advanced prostate cancer
- Metastatic prostate cancer
- Managing complications of disease
- Managing complications of treatment
- Hormonal therapy for prostate cancer

In addition, a NICE pathway on prostate cancer is available from the National Institute for Health and Care Excellence (NICE) Web site .

Scope

Disease/Condition(s)

Prostate cancer

Guideline Category

Counseling

Diagnosis

Evaluation

Management

Risk Assessment

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Nuclear Medicine

Nursing

Oncology

Pharmacology

Psychiatry

Psychology

Radiation Oncology

Surgery

Urology

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

Guideline Objective(s)

To offer best practice advice on the care of men referred to secondary care with suspected or diagnosed prostate cancer, including follow-up in primary care for men with diagnosed prostate cancer

Target Population

Men referred from primary care for investigation of possible prostate cancer and men with a biopsy-proven diagnosis of primary adenocarcinoma of the prostate, or an agreed clinical diagnosis if biopsy is inappropriate

Note: The guideline does not cover asymptomatic men with an abnormal PSA level detected in primary care who are not referred for subsequent investigation, men with metastatic disease of different primary origin involving the prostate, and men with rare malignant tumours of the prostate, such as small cell carcinoma and rhabdomyosarcoma.

Interventions and Practices Considered

Diagnosis/Evaluation/Risk Assessment

1. Prostate biopsy
2. Multiparametric magnetic resonance imaging (MRI) for rebiopsy
3. Staging, including risk stratification based on prostate specific antigen (PSA) level, Gleason score, and clinical stage
4. Computed tomography (CT) based on risk
5. Isotope bone scans based on risk
6. Positron emission tomography (not recommended routinely)
7. Use of nomograms

8. Assessment of fracture risk

Management/Treatment

1. Information and decision support for men with prostate cancer and their carers
2. Counseling on side effects of treatment (altered sexual and urinary function, loss of fertility)
3. Urological assessment
4. Active surveillance
5. Radical treatment
    - Radical prostatectomy
    - Radical radiotherapy
    - Radical external beam radiotherapy
    - Androgen deprivation therapy
    - Brachytherapy
    - Combination therapy
    - High-intensity focused ultrasound and cryotherapy (as part of clinical trials)
6. Watchful waiting
7. Pelvic radiotherapy
8. Adjuvant hormonal therapy
9. Managing adverse effects of radical treatment
    - Phosphodiesterase type 5 (PDE5) inhibitors, vacuum devices, intraurethral inserts, penile injections, or penile prostheses for impotence
    - Urinary incontinence coping strategies, pelvic floor muscle re-education, bladder retraining, pharmacotherapy, and artificial urinary sphincter for urinary incontinence
    - Investigation of radiation-induced enteropathy
10. Managing relapse after radical treatment
    - Analysis of serial PSA levels
    - Biopsy
    - Isotope bone scan
    - Radical radiotherapy to the prostatic bed
    - Entry to appropriate clinical trials
    - Hormonal therapy
11. Managing adverse effects of hormone therapy
    - Medroxyprogesterone, cyproterone acetate, and megestrol acetate for hot flushes
    - Sperm storage for infertility
    - PDE5 inhibitors, intraurethral inserts, penile injections, penile prostheses, and vacuum devices for impotence
    - Bisphosphonates and denosumab for osteoporosis
    - Prophylactic radiotherapy and tamoxifen for gynaecomastia
    - Resistance and aerobic exercise for fatigue
12. Bilateral orchidectomy
13. Continuous luteinising hormone-releasing hormone agonist therapy
14. Bicalutamide monotherapy
15. Docetaxel
16. Corticosteroid therapy (dexamethasone)
17. Strontium-89 for bone metastases
18. Percutaneous nephrostomy or insertion of a double-J stent for obstructive uropathy

Major Outcomes Considered

- Prognostic value of diagnostic tests (reliability, validity, and limitations)
- Symptomatic improvement
- Quality of life
- Adverse effects
- Mortality

- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Developing Clinical Evidence-based Questions

Background

Clinical guidelines should be aimed at changing clinical practice and should avoid ending up as 'evidence-based textbooks' or making recommendations on topics where there is already agreed clinical practice. Therefore the list of key clinical issues listed in the scope were developed in areas that were known to be controversial or uncertain, where there was identifiable practice variation, or where NICE guidelines were likely to have most impact.

Method

From each of the key clinical issues identified in the scope, the Guideline Development Group (GDG) formulated a clinical question. For clinical questions about interventions, the PICO framework was used. This structured approach divides each question into four components: P – the population (the population under study), I – the interventions (what is being done), C – the comparison (other main treatment options), O – the outcomes (the measures of how effective the interventions have been). Where appropriate, the clinical questions were refined once the evidence had been searched and, where necessary, sub-questions were generated.

Review of Clinical Literature

Scoping Search

An initial scoping search for published guidelines, systematic reviews, economic evaluations and ongoing research was carried out on the following databases or websites: NHS Evidence, Cochrane Databases of Systematic Reviews (CDSR), Health Technology Assessment Database (HTA), NHS Economic Evaluations Database (NHS EED), Medline and EMBASE. At the beginning of the development phase, initial scoping searches were carried out to identify any relevant guidelines (local, national or international) produced by other groups or institutions.

Developing the Review Protocol

For each clinical question, the information specialist and researched (with input from other technical team and GDG members) prepared a review protocol This protocol explains how the review was to be carried out (see Table 1 in the full version of the original guideline document) in order to develop a plan of how to review the evidence, limit the introduction of bias and for the purposes of reproducibility. All review protocols can be found in the evidence review.

Searching for the Evidence

In order to answer each question the NCC-C information specialist developed a search strategy to identify relevant published evidence for both clinical and cost effectiveness. Key words and terms for the search were agreed in collaboration with the GDG. When required, the health economist searched for supplementary papers to inform detailed health economic work (see section on 'Incorporating Health Economic Evidence' in the full version of the original guideline document). For those clinical topics that were updated from the 2008 guideline, searches were set to only identify evidence published after June 2007 to ensure no relevant papers were missed. No date limits were applied to searches carried on new topics within the 2014 guideline. Search filters, such as those to identify systematic reviews (SRs) and randomised controlled trials (RCTs) were applied to the search strategies when necessary. No language restrictions were applied to the search; however, foreign language papers were not

requested or reviewed (unless of particular importance to that question).

The following databases were included in the literature search:

- The Cochrane Library
- Medline and PreMedline 1946 onwards
- Excerpta Medica (EMBASE) 1974 onwards
- Web of Science (specifically Science Citation Index Expanded [SCI-EXPANDED] 1899 onwards and Social Sciences Citation Index [SSCI] 1956 onwards)
- System for Information on Grey Literature In Europe (SIGLE) 1980–2005
- Biomed Central 1997 onwards

Subject specific databases used for certain topics:

- Cumulative Index to Nursing and Allied Health Literature (CINAHL) 1937 onwards
- Allied & Complementary Medicine (AMED) 1985 onwards
- British Nursing Index (BNI) 1993 onwards
- PsycINFO 1806 onwards

From this list the information specialist sifted and removed any irrelevant material based on the title or abstract before passing to the researcher. All the remaining articles were then stored in a Reference Manager electronic library. Searches were updated and re-run 8–10 weeks before the stakeholder consultation, thereby ensuring that the latest relevant published evidence was included in the database. Any evidence published after this date was not included. For the purposes of updating this guideline, May 2013 should be considered the starting point for searching for new evidence.

Further details of the search strategies, including the methodological filters used, are provided in the evidence review (see Appendix M in the full version of the original guideline document).

Prioritising Topics for Economic Analysis

For each topic, a review of the economic literature was conducted. Where published economic evaluation studies were identified that addressed the economic issues for a clinical question, these are presented alongside the clinical evidence. For those clinical areas reviewed, the information specialists used a similar search strategy as used for the review of clinical evidence but with the inclusion of a health economics filter.

For systematic searches of published economic evidence, the following databases were included:

- Medline
- EMBASE
- NHS EED
- HTA
- Health Economic Evaluations Database (HEED)

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Overall Quality of Outcome Evidence in Grading of Recommendations Assessment, Development and Evaluation (GRADE)

Level	Description
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Critical Appraisal and Evidence Grading

Following the literature search one researcher independently scanned the titles and abstracts of every article for each question, and full publications were obtained for any studies considered relevant or where there was insufficient information from the title and abstract to make a decision. When papers were obtained the researcher applied inclusion/exclusion criteria to select appropriate studies, which were then critically appraised. For each question, data on the type of PICO (population, intervention, comparison and outcome) were extracted and recorded in evidence tables and an accompanying evidence summary prepared for the Guideline Development Group (GDG). All evidence was considered carefully by the GDG for accuracy and completeness.

Grading of Recommendations, Assessment, Development and Evaluation (GRADE)

For interventional questions, studies which matched the inclusion criteria were evaluated and presented using a modification of GRADE (http://gradeworkinggroup.org/). Where possible this included meta-analysis and synthesis of data into a GRADE 'evidence profile'. The evidence profile shows, for each outcome, an overall assessment of both the quality of the evidence as a whole (very low, low, moderate or high) as well as an estimate of the size of effect. A narrative summary (evidence statement) was also prepared. Each topic outcome was examined for the quality elements defined in Table 1 in the full version of the original guideline document, and subsequently graded using the quality levels listed in the "Rating Scheme for the Strength of the Evidence" field. The reasons for downgrading or upgrading specific outcomes were explained in footnotes.

All procedures were fully compliant with NICE methodology as detailed in the 'NICE Guidelines Manual' (see the "Availability of Companion Documents" field). In general, no formal contact was made with authors; however, there were ad hoc occasions when this was required in order to clarify specific details. For non-interventional questions, for example the questions regarding diagnostic test accuracy, a narrative summary of the quality of the evidence was given. The quality of individual diagnostic accuracy studies was assessed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool.

Incorporating Health Economics Evidence

The aim of providing economic input into the development of the guideline was to inform the GDG of potential economic issues relating to prostate cancer. Health economics is about improving the health of the population through the efficient use of resources. In addition to assessing clinical effectiveness, it is important to investigate whether health services are being used in a cost effective manner in order to maximise health gain from available resources.

Methods for Reviewing and Appraising Economic Evidence

The aim of reviewing and appraising the existing economic literature is to identify relevant economic evaluations that compare both costs and health consequences of alternative interventions and that are applicable to National Health Service (NHS) practice. Thus studies that only report costs, non-comparative studies of 'cost of illness' studies are generally excluded from the reviews.

Economic studies identified through a systematic search of the literature are appraised using a methodology checklist designed for economic evaluations (see Appendix H in the full version of the original guideline document). This checklist is not intended to judge the quality of a study per se, but to determine whether an existing economic evaluation is useful to inform the decision-making of the GDG for a specific topic within the guideline. There are two parts of the appraisal process; the first step is to assess applicability (i.e., the relevance of the study to the specific guideline topic and the NICE reference case) (see Table 4 in the full version of the original guideline document). In the second step, only those studies deemed directly or partially applicable are further assessed for limitations (i.e., the methodological quality, see Table 5 in the full version of the original guideline document).

Where relevant, a summary of the main findings from the systematic search, review and appraisal of economic evidence is presented in an economic evidence profile alongside the clinical evidence.

If high-quality published economic evidence relevant to current NHS practice was identified through the search, the existing literature was reviewed and appraised as described above. However, it is often the case that published economic studies may not be directly relevant to the specific clinical question as defined in the guideline or may not be comprehensive or conclusive enough to inform UK practice. In such cases, for priority topics, consideration was given to undertaking a new economic analysis as part of this guideline.

Economic Modelling

Once the need for a new economic analysis for high priority topics had been agreed by the GDG, the health economist investigated the feasibility of developing an economic model. In the development of the analysis, the following general principles were adhered to:

- The GDG subgroup was consulted during the construction and interpretation of the analysis
- The analysis was based on the best available clinical evidence from the systematic review
- Assumptions were reported fully and transparently
- Uncertainty was explored through sensitivity analysis
- Costs were calculated from a health services perspective
- Outcomes were reported in terms of quality-adjusted life years

Methods Used to Formulate the Recommendations

Expert Consensus

Expert Consensus (Delphi)

Informal Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

The Guideline Development Group (GDG)

The prostate cancer GDG was recruited in line with the "NICE guidelines manual" (NICE 2009, 2012). The first step was to appoint a Chair and a Lead Clinician. Advertisements were placed for both posts and shortlisted candidates were interviewed by telephone prior to being offered the role. The NCC-C Director, GDG Chair and Lead Clinician identified a list of specialties that needed to be represented on the GDG. Details of the adverts were sent to the main stakeholder organisations, cancer networks and patient organisations/charities (see Appendix I in the full version of the original guideline document). Individual GDG members were selected by the NCC-C Director, GDG Chair and Lead Clinician, based on their application forms. The guideline development process was supported by staff from the NCC-C, who undertook the clinical and health economics literature searches, reviewed and presented the evidence to the GDG, managed the process and contributed to drafting the guideline. At the start

of the guideline development process all GDG members' interests were recorded on a standard declaration form that covered consultancies, fee-paid work, share-holdings, fellowships and support from the healthcare industry. At all subsequent GDG meetings, members declared new, arising conflicts of interest which were always recorded (see Appendix I in the full version of the original guideline document).

Guideline Development Group Meetings

Ten GDG meetings were held between 9-10 February 2012 and 1-2 May 2013. During each GDG meeting (held over either 1 or 2 days) clinical questions and clinical and economic evidence were reviewed, assessed and recommendations formulated. At each meeting patient/carer and service-user concerns were routinely discussed as part of a standing agenda item. NCC-C project managers divided the GDG workload by allocating specific clinical questions, relevant to their area of clinical practice, to small sub-groups of the GDG in order to simplify and speed up the guideline development process. These groups considered the evidence, as reviewed by the researcher, and synthesised it into draft recommendations before presenting it to the GDG. These recommendations were then discussed and agreed by the GDG as a whole. Each clinical question was led by a GDG member with expert knowledge of the clinical area (usually one of the healthcare professionals). The GDG subgroups often helped refine the clinical questions and the clinical definitions of treatments. They also assisted the NCC-C team in drafting the section of the guideline relevant to their specific topic.

Patient/Carer Representatives

Individuals with direct experience of prostate cancer services gave an important user focus to the GDG and the guideline development process. The GDG included two patient/carer members. They contributed as full GDG members to writing the clinical questions, helping to ensure that the evidence addressed their views and preferences, highlighting sensitive issues and terminology relevant to the guideline and bringing service-user research to the attention of the GDG.

Modified Delphi Consensus Methodology

The NCC-C technical team conducted a survey of UK active surveillance protocols for prostate cancer which indicated a need for a standardised protocol. However the GDG felt that due to the lack of published evidence about the relative effectiveness of active surveillance protocols any such recommendations could not be implemented without first seeking consensus within the prostate cancer community. For this reason the group decided to use a modified Delphi formal process to seek consensus about the ideal active surveillance protocol for men with low risk localised prostate cancer. The GDG invited 210 health professionals and patients to participate in the consensus process. One hundred fifty-two respondents took part in round one, 120 in round two and 102 in round three. Following three rounds, consensus (defined as agreement between at least two thirds of respondents) was reached on several components of the active surveillance protocol. The protocol and results of the Delphi consensus process are in Appendix C of the evidence review in the full version of the original guideline document.

Needs Assessment

As part of the guideline development process the NCC-C undertook a needs assessment. This aims to describe the burden of disease and current service provision for men with prostate cancer in England and Wales, and informed the development of the guideline. Assessment of the effectiveness of interventions is not included in the needs assessment, and was undertaken separately by researchers in the NCC-C as part of the guideline development process. The information included in the needs assessment document was presented to the GDG. Most of the information was presented early in the stages of guideline development, and other information was included to meet the evolving information needs of the GDG during the course of guideline development.

Prioritising Topics for Economic Analysis

After the clinical questions had been defined, and with the help of the health economist, the GDG discussed and agreed which of the clinical questions were potential priorities for economic analysis. These economic priorities were chosen on the basis of the following criteria, in broad accordance with the NICE guidelines manual (NICE 2009, 2012):

- The overall importance of the recommendation, which may be a function of the number of patients affected and the potential impact on costs and health outcomes per patient
- The current extent of uncertainty over cost effectiveness, and the likelihood that economic analysis will reduce this uncertainty
- The feasibility of building an economic model

Agreeing the Recommendations

For each clinical question the GDG were presented with a summary of the clinical evidence, and, where appropriate, economic evidence, derived from the studies reviewed and appraised. From this information the GDG were able to derive the guideline recommendations. The link between the evidence and the view of the GDG in making each recommendation is made explicitly in the accompanying LETR statement (see below).

Wording of the Recommendations

The wording used in the recommendations in this guideline denotes the certainty with which the recommendations were made. Some recommendations were made with more certainty than others. Recommendations are based on the trade-off between the benefits and harms of an intervention, whilst taking into account the quality of the underpinning evidence. For all recommendations, it is expected that a discussion will take place with the patients about the risks and benefits of the interventions, and their values and preferences. This discussion should help the patient reach a fully informed decision. Terms used within this guideline are:

- 'Offer' – for the vast majority of patients, an intervention will do more good than harm
- 'Do not offer' – the intervention will not be of benefit for most patients
- 'Consider' – the benefit is less certain, and an intervention will do more good than harm for most patients. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for an 'offer' recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

LETR (Linking Evidence to Recommendations) Statements

As clinical guidelines were previously formatted, there was limited scope for expressing how and why a GDG made a particular recommendation from the evidence of clinical and cost effectiveness. Recommendations in the 2008 guideline were accompanied by a 'qualifying statement' which stated the level of evidence the recommendations were based on. To make this process more transparent to the reader, NICE have introduced an explicit, easily understood and consistent way of expressing the reasons for making each recommendation. This is known as the 'LETR statement' and will usually cover the following key points:

- The relative value placed on the outcomes considered
- The strength of evidence about benefits and harms for the intervention being considered
- The costs and cost-effectiveness of an intervention
- The quality of the evidence (see GRADE)
- The degree of consensus within the GDG
- Other considerations – for example equalities issues

Where evidence was weak or lacking the GDG agreed the final recommendations through informal consensus. Shortly before the consultation period, ten key priorities and five key research recommendations were selected by the GDG for implementation and the patient algorithms were agreed.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GDG usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally 'must' (or 'must not') is used if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost-effective. Similar forms of words (for example, 'Do not offer…') are used when the GDG is confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost-effective, but other options may be similarly cost-effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and

discussing the options with the patient.

Recommendation Wording in Guideline Updates

The National Institute for Health and Care Excellence (NICE) began using this approach to denote the strength of recommendations in guidelines that started development after publication of the 2009 version of 'The guidelines manual' (January 2009). This does not apply to any recommendations ending [2008]. In particular, for recommendations labelled [2008] the word 'consider' may not necessarily be used to denote the strength of the recommendation.

Cost Analysis

See the following appendices in the full version of the original guideline document:

- Appendix B: The cost-effectiveness of multiparametric magnetic resonance imaging (mpMRI) before trans-rectal ultrasound (TRUS) guided prostate biopsy in men with suspected prostate cancer
- Appendix D: An economic evaluation of radical prostatectomy versus alternative treatment options for clinically localised prostate cancer
- Appendix E: The cost-effectiveness of high-dose rate (HDR) brachytherapy in combination with external beam radiotherapy alone

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Consultation and Validation of the Guideline

The draft of the guideline was prepared by National Collaborating Centre for Cancer (NCC-C) staff in partnership with the Guideline Development Group (GDG) Chair and Lead Clinician. This was then discussed and agreed with the GDG and subsequently forwarded to the National Institute for Health and Care Excellence (NICE) for consultation with stakeholders.

Registered stakeholders (see Appendix I in the full version of the original guideline document) had one opportunity to comment on the draft guideline which was posted on the NICE website between 16 July 2013 and 10 September 2013 in line with NICE methodology (NICE 2012).

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate diagnosis and treatment of prostate cancer

Potential Harms

- There is a small increase in the risk of colorectal cancer after radical external beam radiotherapy for prostate cancer.
- Use caution when performing anterior wall rectal biopsy after brachytherapy because of the risk of fistulation.

- Adverse effects of hormone therapy (hot flushes, sexual dysfunction, osteoporosis, gynaecomastia, fatigue)
- Adverse effects of radical treatment (sexual dysfunction, urinary incontinence, radiation-induced enteropathy, relapse)

See the "Trade-off between clinical benefits and harms" sections in the full guideline document for details about harms of specific interventions.

Contraindications

Contraindications

Clinical or radiological evidence of T3 disease is usually a contraindication to radical surgery; however, men with T3 cancers are sometimes treated with radical prostatectomy. The appropriate extent of lymphadenectomy and its influence on survival is uncertain.

Qualifying Statements

Qualifying Statements

- This guidance represents the view of National Institute for Health and Care Excellence (NICE), which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summaries of product characteristics of any drugs.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.
- Healthcare professionals are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.
- The guideline assumes that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.
- This guideline recommends some drugs for indications for which they do not have a UK marketing authorisation at the date of publication, if there is good evidence to support that use. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or those with authority to give consent on their behalf) should provide informed consent, which should be documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information. Where recommendations have been made for the use of drugs outside their licensed indications ('off-label use'), these drugs are marked with a footnote in the recommendations.
- Patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If the patient is under 16, their family or carers should also be given information and support to help the child or young person to make decisions about their treatment.
- Healthcare professionals should follow the Department of Health's advice on consent. If someone does not have capacity to make decisions, healthcare professionals should follow the code of practice that accompanies the Mental Capacity Act and the supplementary code of practice on deprivation of liberty safeguards. NICE has produced guidance on the components of good patient experience in adult NHS services. All healthcare professionals should follow the recommendations in Patient experience in adult NHS services.
- For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision (see also 'Patient-centred Care' in the original guideline document).

Implementation of the Guideline

Description of Implementation Strategy

Implementation tools and resources to help you put the guideline into practice are available from the National Institute for Health and Care Excellence (NICE) website (see also the "Availability of Companion Documents" field).

Key Priorities for Implementation

The following recommendations have been identified as priorities for implementation.

Information and Decision Support for Men With Prostate Cancer, Their Partners and Carers

Decision Support

Discuss all relevant management options recommended in this guideline with men with prostate cancer and their partners or carers, irrespective of whether they are available through local services. [2008]

Assessment

Diagnosis

Magnetic Resonance Imaging (MRI) for Rebiopsy

Consider multiparametric MRI (using T2- and diffusion-weighted imaging) for men with a negative transrectal ultrasound 10–12 core biopsy to determine whether another biopsy is needed. [new 2014]

Staging

Consider multiparametric MRI, or computed tomography (CT) if MRI is contraindicated, for men with histologically proven prostate cancer if knowledge of the T or N stage could affect management. [new 2014]

Localised and Locally Advanced Prostate Cancer

Low-risk Localised Prostate Cancer

Active Surveillance

Offer active surveillance (in line with the following recommendation) as an option to men with low-risk localised prostate cancer for whom radical prostatectomy or radical radiotherapy is suitable. [new 2014]

Consider using the protocol in the table below for men who have chosen active surveillance. [new 2014]

Table. Protocol for Active Surveillance

Timing	Tests*
At enrolment in active surveillance	Multiparametric magnetic resonance imaging (MRI) if not previously performed
Year 1 of active surveillance	• Every 3–4 months: measure prostate-specific antigen (PSA)† • Throughout active surveillance: monitor PSA kinetics‡ • Every 6–12 months: digital rectal examination (DRE)¶ • At 12 months: prostate rebiopsy
Years 2–4 of active surveillance	• Every 3–6 months: measure PSA† • Throughout active surveillance: monitor PSA kinetics‡ • Every 6–12 months: DRE¶
Year 5 and every year thereafter until active surveillance ends	• Every 6 months: measure PSA† • Throughout active surveillance: monitor PSA kinetics‡

Timing	Tests*Every 12 months: DRE¶

*If there is concern about clinical or PSA changes at any time during active surveillance, reassess with multiparametric MRI and/or rebiopsy.

†May be carried out in primary care if there are agreed shared-care protocols and recall systems.

‡May include PSA doubling time and velocity.

¶Should be performed by a healthcare professional with expertise and confidence in performing DRE.

Intermediate- and High-risk Localised Prostate Cancer

Active Surveillance

Consider active surveillance (in line with the recommendation above) for men with intermediate-risk localised prostate cancer who do not wish to have immediate radical prostatectomy or radical radiotherapy. [new 2014]

Radical Treatment

Offer men with intermediate- and high-risk localised prostate cancer a combination of radical radiotherapy and androgen deprivation therapy, rather than radical radiotherapy or androgen deprivation therapy alone. [new 2014]

Managing Adverse Effects of Radical Treatment

Sexual Dysfunction

Ensure that men have early and ongoing access to specialist erectile dysfunction services. [2008, amended 2014]

Radiation-induced Enteropathy

Ensure that men with signs or symptoms of radiation-induced enteropathy are offered care from a team of professionals with expertise in radiation-induced enteropathy (who may include oncologists, gastroenterologists, bowel surgeons, dietitians and specialist nurses). [new 2014]

Men Having Hormone Therapy

Consider intermittent therapy for men having long-term androgen deprivation therapy (not in the adjuvant setting), and include discussion with the man, and his partner, family or carers if he wishes, about:

- The rationale for intermittent therapy and
- The limited evidence for reduction in side effects from intermittent therapy and
- The effect of intermittent therapy on progression of prostate cancer [new 2014]

Implementation Tools

Audit Criteria/Indicators

Clinical Algorithm

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Collaborating Centre for Cancer. Prostate cancer: diagnosis and treatment. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Jan. 46 p. (Clinical guideline; no. 175).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2008 Feb (revised 2014 Jan)

Guideline Developer(s)

National Collaborating Centre for Cancer - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Guideline Development Group (GDG)

Composition of Group That Authored the Guideline

Guideline Development Group Members: Hugh Butcher, Patient and carer member; Sarah Cant, Patient and carer member, Head of Policy and Campaigns, Prostate Cancer UK; Sean Duffy (*GDG Chair*) (until March 2013), Yorkshire Cancer Network; John Graham (*GDG Chair*) (from March 2013), Consultant Lead Clinical Oncologist, Taunton and Somerset NHS Trust; Peter Hoskin, Consultant Oncologist, Mount Vernon Cancer Centre; Nicola James, Nurse Consultant, Chesterfield Royal Hospital, Derbyshire; Peter Kirkbride, GDG Lead Clinician, Medical Director, Clatterbridge Cancer Centre, Merseyside; Howard Kynaston, Professor of Urological Surgery, Cardiff University; Brian McGlynn, Nurse Consultant Urology Oncology, The Ayr Hospital, Ayr; David Neal, Professor of Surgical Oncology, University of Cambridge; Kathleen Nuttall, Director, Lancashire and South Cumbria Cancer Network; Jon Oxley, Consultant in Cellular Pathology, Southmead Hospital, Bristol;

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Financial Disclosures/Conflicts of Interest

At the start of the guideline development process all Guideline Development Group (GDG) members' interests were recorded on a standard declaration form that covered consultancies, fee-paid work, share-holdings, fellowships and support from the healthcare industry. At all subsequent GDG meetings, members declared new, arising conflicts of interest which were always recorded (see Appendix I in the full version of the original guideline document).

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Collaborating Centre for Cancer. Prostate cancer: diagnosis and treatment. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Feb. 146 p. (NICE clinical guideline; no. 58).

Guideline Availability

Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site .

Availability of Companion Documents

The following are available:

- Prostate cancer: diagnosis and treatment. Full guideline. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Jan. 480 p. (Clinical guideline; no. 175). Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Care Excellence (NICE) Web site .
- Prostate cancer: diagnosis and treatment. Full guideline appendices J-L. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Jan. 223 p. (Clinical guideline; no. 175). Electronic copies: Available in PDF from the NICE Web site .
- Prostate cancer: diagnosis and treatment. Full guideline appendix M. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Jan. 1345 p. (Clinical guideline; no. 175). Electronic copies: Available in PDF from the NICE Web site .
- Prostate cancer: diagnosis and treatment. Costing statement. London (UK): National Institute for Health and Care Excellence; 2014 Jan 11 p. (Clinical guideline; no. 175). Electronic copies: Available in PDF from the NICE Web site .
- Prostate cancer: diagnosis and treatment. Clinical audit tool. London (UK): National Institute for Health and Care Excellence; 2014 Jan. 10 p. (Clinical guideline; no. 175). Electronic copies: Available in PDF from the NICE Web site .
- Prostate cancer: diagnosis and treatment. Baseline assessment tool. London (UK): National Institute for Health and Care Excellence; 2014 Jan. 10 p. (Clinical guideline; no. 175). Electronic copies: Available from the NICE Web site .
- Prostate cancer: protocol for active surveillance. London (UK): National Institute for Health and Care Excellence; 2014 Jan. 2 p. (Clinical guideline; no. 175). Electronic copies: Available from the NICE Web site .
- The guidelines manual 2009. London (UK): National Institute for Health and Care Excellence (NICE); 2009 Jan. Electronic copies: Available in PDF from the NICE Archive Web site .
- The guidelines manual 2012. London (UK): National Institute for Health and Care Excellence (NICE); 2012 Jan. Electronic copies: Available in PDF from the NICE Archive Web site .

Patient Resources

The following is available:

- Prostate cancer: diagnosis and treatment. Information for the public. London (UK): National Institute for Health and Care Excellence

(NICE); 2014 Jan. (Clinical guideline; no. 175). Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download as a Kindle or EPUB ebook from the NICE Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This summary was completed by ECRI Institute on September 22, 2009. This summary was updated by ECRI Institute on May 5, 2014. This summary was updated by ECRI Institute on July 18, 2014 following the U.S. Food and Drug Administration advisory on Docetaxel.

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